Animal Reproduction Science 153 (2015) 8–12

Contents lists available at ScienceDirect

Animal Reproduction Science

journal homepage: www.elsevier.com/locate/anireprosci

Luteal changes after treatment with sub-luteolytic doses of prostaglandin (cloprostenol sodium) in cattle

Eduardo Trevisol[a], Jair Camargo Ferreira[a], Camila Louise Ackermann[a], Flavia Caroline Destro[a], Wolff Camargo Marques Filho[a], Aline Souza Carmagos[a], Marcos Vinicius Biehl[c], Jackson Barros do Amaral[d], José Carlos de Figueiredo Pantoja[b], Roberto Sartori[c], João Carlos Pinheiro Ferreira[a,*]

[a] Department of Animal Reproduction and Veterinary Radiology, School of Veterinary Medicine and Animal Science, Univ. Estadual Paulista-FMVZ, Unesp, Botucatu, SP, Brazil
[b] Department of Veterinary Hygiene and Public Health, School of Veterinary Medicine and Animal Science, Univ. Estadual Paulista-FMVZ, Unesp, Botucatu, SP, Brazil
[c] Department of Animal Science, ESALQ, University of São Paulo (USP), Piracicaba, SP, Brazil
[d] Institute of Animal Science, SAA, Nova Odessa, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 8 March 2014
Received in revised form
18 November 2014
Accepted 3 December 2014
Available online 26 December 2014

Keywords:
Cow
Corpus luteum
Partial luteolysis

ABSTRACT

This study characterizes the physiological and morphological changes related to partial luteolysis in bovine corpus luteum (CL) after challenges with sub-doses of cloprostenol sodium on Day 6 (D6) of the estrous cycle. Cows (n = 12/treatment) were treated as follows: Control (2 mL, saline, i.m.); 2XPGF (two treatments i.m. 500 μg of cloprostenol sodium 2 h apart) and 1/6PGF (83.3 μg of cloprostenol sodium, i.m., once). Plasma progesterone (P4) concentration, CL volume and blood flow were measured immediately before the treatments, then every 8 h (h) for 48 h. In the Control, P4 concentrations were higher at 48 h than at 0 h. P4 decreased 8 h after 2XPGF treatment ($P < 0.05$), and remained low until the end of the trial. P4 decreased in 1/6PGF between 8 and 16 h ($P < 0.05$), then began to rebound at 24 h. Luteal volume was higher in Controls at 48 h than at 0 h. Under 1/6PGF, luteal volume decreased at 24 h ($P < 0.05$) and began to rebound at 32 h. Luteal volume and blood flow were reduced starting at 24 and 32 h, respectively, after 2XPGF treatment ($P < 0.05$). In this study, we were able to describe the partial luteolysis phenomenon, induced by a treatment of a D6CL with cloprostenol sub-dose.

1. Introduction

The corpus luteum (CL) is a temporary gland formed in the ovary after ovulation, which secretes progesterone (P4) to regulate the estrous cycle and to help to maintain pregnancy (Niswender et al., 2000). In the absence of pregnancy, CL regression occurs after 4–8 pulses of endometrial PGF2α release in a 6–14 h period (Kindahl et al., 1976; Silvia et al., 1991; Mann and Lamming, 2006).

Because its luteolitic action, PGF2α or its synthetic analog cloprostenol have been used from Day 5 (D5) (Ribeiro et al., 2012; Santos et al., 2010) to D7 of the estrous cycle (Giordano et al., 2013; Santos et al., 2010) to induce luteolysis in timed artificial insemination protocols.

* Corresponding author at: Department of Animal Reproduction and Veterinary Radiology, FMVZ, Univ. Estadual Paulista, Distrito de Rubião Junior s/n, Botucatu, São Paulo, Brazil. Tel.: +55 14 38802121.
E-mail address: jcferreira@fmvz.unesp.br (J.C.P. Ferreira).

http://dx.doi.org/10.1016/j.anireprosci.2014.12.005
0378-4320/

Considering the classical definitions of luteolysis (circulating P4 concentration < 1 ng/mL 24–72 h after PGF2α treatment), the CL regression rate in Holstein cows varies from 45.7% to 51.7% with one PGF2α treatment on D5 (respectively, Ribeiro et al., 2012; Santos et al., 2010), 96% to 97.9% (two PGF2α treatments on D5 and D6 – Santos et al., 2010) and 71.4% to 86.8% (one PGF2α treatment on D7 – Santos et al., 2010).

However, Nascimento et al. (2014), despite having observed mean P4 circulanting concentration ≤ 1 ng/mL in nonlactanting Holstein cows at 12 and 24 h after PGF2α treatment on D5 using one, two or double doses, they found that 10 days after treatment, all cows had P4 concentrations > 1 ng/mL and a functional CL, showing that the treatment was insufficient to induce complete luteolysis.

The term partial luteolysis was first reported by Stellflug et al. (1977) that treated hysterectomized cows with 5 mg or 10 mg of PGF2α (10% or 20% of label doses, respectively) and observed that circulating P4 dropped during the first 12 h after treatment but after that, it declined little during the next 4 days or even rebounded.

This phenomenon was also described by Meira et al. (2006) in Nelore cows treated on D9 of the estrous cycle with 50% or 25% of the recommended conventional dose (15 mg) of luprostiol and observed that several cows that had received 50% or 25% of the conventional dose showed a decrease in plasma P4 concentration to values close to 1.0 ng/mL at 24 h. However, 48 h after the treatments, P4 rebounded.

Ginther et al. (2009) and Shrestha et al. (2010) reported a similar phenomenon in Holstein heifers treated with intravenous or intrauterine dinoprost tromethamine (0.5 mg or 1.0 mg) pulses, and named it as partial luteolysis. The heifers showed an initial decrease of circulating P4 concentration between 6 and 12 h after treatment, followed by an increase in values similar to those observed before the treatment.

In a trial conducted in our laboratory, seven Caracu cows were treated with 83.33 μg of cloprostenol sodium on D6 and all but one presented partial luteolysis, that was characterized by the drop of circulating P4 concentrations to ~1.0 ng/mL between 16 and 24 h after treatment followed by a rebound (Trevisol, 2011).

Considering the importance of understanding the mechanism related to the partial luteolysis in cattle, and based on our previous results that 83.33 μg of cloprostenol induces this phenomenon at D6 of the estrous cycle, the present study aimed to characterize the P4 and morphological changes in bovine CL after challenges with sub-doses of a PGF2α analog (cloprostenol sodium).

2. Materials and methods

2.1. Cows

This study was conducted, from July 2011 to July 2012, at the Institute of Animal Science in Nova Odessa, São Paulo, Brazil (22°46′S; 47°17′W), whose Ethics Committee had approved the experimental design (Protocol number: 119). Twelve clinically healthy estrous cycling Caracu cows, at least 6 months postpartum, 5–7 years old, and presenting a body condition score ≥3.5 (0–5 point scale; Houghton et al., 1990) were used. Cows were kept in paddocks where they were fed grass supplemented with hay and concentrate, once daily, and had access to mineral supplement and water *ad libitum*.

2.2. Ovulation synchronization

After a 30-day period of adaptation to the experimental conditions, specifically to the manipulation team and the procedures, estrous cycles were synchronized by administration of 50 μg GnRH i.m. (lecirelin – Gestran Plus®; Tecnopec Ltd, São Paulo, Brazil) and insertion of an intravaginal device impregnated with 1 g of P4 (Primer® – Tecnopec Ltd, São Paulo, Brazil). Then, 6.5 days (d) later, 500 μg of PGF2α was given i.m. (cloprostenol sodium, Sincrocio®; OuroFino Agribusiness, Riberão Preto, Brazil) and 12 h later, a second PGF2α treatment with 250 μg was given and the P4 intravaginal device was withdrawn. Two days after the second PGF2α, 50 μg of GnRH was administered i.m.

Ovaries were examined every 12 h by transrectal ultrasonography (Aloka SSD 500; Aloka Co. Ltd, Tokyo, Japan, with a 5.0-MHz transducer) after the second GnRH administration (D0) for monitoring the time of ovulation, that occurred between 24 and 32 h after the second GnRH.

2.3. Experimental procedures

On D6, the cows were randomly assigned to one of three groups of four and underwent three treatments in a Latin square design as follows:

- *Control*: 2 mL of saline (0.9% NaCl),
- *2XPGF*: 2 × 500 μg of cloprostenol sodium 2 h apart, and
- *1/6PGF*: 83.33 μg of cloprostenol sodium.

All treatments were injected into the semitendinosus muscle at 8 a.m. These procedures were repeated three times so that all cows were subjected to all treatments. There was a month interval between each repetition.

Blood samples were collected into heparinized tubes using indwelling jugular catheters. Before the catheterization, the cows were lightly sedated with 25 mg/cow of xylazine hydrochloride i.m. (Anasedan, Vetbrands International, Inc., Miramar, FL, USA).

Samples for measurement of plasma P4 concentration were collected immediately before (Hour zero – H0) and then every 8 h until 48 h after the treatments. After collection, samples were centrifuged and the plasma was harvested and frozen at −20 °C.

2.4. Ultrasonography

Starting at Hour 0 and then every 8 h until 48 h after treatments, CL transrectal ultrasonography examinations were performed using a portable ultrasound device (SONOACE PICO, Samsung Medison, New Jersey, USA), equipped with a 5–9 MHz, linear-array transducer (LV5-9CDn, 60 mm). At each examination, two orthogonal cross-sectional luteal images with maximal areas were